REMARKS

Claims 1-26 were pending in the present application.

Claims 14-20 have been canceled without prejudice. Applicant reserves the right to pursue any deleted subject matter in one or more continuing applications.

After entry of the amendments, claims 1-13 and 21-26 will be pending.

Applicant respectfully requests entry of the foregoing amendments and consideration of the following remarks.

Claim Rejections – 35 U.S.C. § 103

Claims 1-12 and 21-26 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over WO 96/04932 ("Balasubramanian") in view of WO 97/25072 ("Engler"). Applicants respectfully traverse.

The Examiner has contended that it would have been *prima facie* obvious to the skilled artisan at the time of the present invention to include a cationic detergent in the compositions of Balasubramanian comprising polynucleotides, a high molecular weight block copolymer adjuvant, and optionally a nonionic surfactant, in order to enhance delivery of polynucleotides because (1) one of skill in the art would have been motivated to use a cationic detergent to enhance delivery of a nucleic acid as taught by Engler; and (2) there would have been a reasonable expectation of success based on the high degree of skill in molecular biology and the detailed disclosures of Balasubramanian and Engler.

In response to Applicant's argument that Engler teaches away from combining a cationic surfactant with a high molecular weight block copolymer such as CRL-1005 by showing that neither benzalkonium chloride nor cetylpyridium enhanced gene transfer, the Examiner noted that Engler was cited to supplement Balasubramanian by "teaching that cationic detergents, a class of surfactants, can enhance the delivery of nucleic acids to cells" and that Engler "clearly shows positive gene transfer using DNA in the form of recombinant adenoviral vector and the cationic surfactants benzalkonium chloride and cetylpyridium."

Applicant respectfully disagrees with the Examiner's interpretation of Engler and reiterates the position that Engler teaches away from the present invention. First, Engler does not clearly show that positive gene transfer occurs using recombinant adenoviral vector and cationic surfactants. Example 5 in Engler describes the staining of bladders treated with a recombinant

adenoviral vector. See Engler, pg. 13, lines 22-29. In particular, the stained bladders were scored into three categories: + (minimal staining), ++ (moderate staining) or +++ (intense staining covering the whole bladder epithelial surface. See id, pg. 13, lines 29-31. Notably, there is no negative control in the experiment and no provision for a score indicative of less than minimal staining. This would indicate that a score of "+" is equivalent to background. Thus, in Table 1 where gene expression in bladder epithelium was categorized as "+" for cetylpyridium and "<+" for benzalkonium chloride, the skilled artisan would understand that the staining was equivalent to background and would conclude that no enhancement of gene transfer had occurred.

Second, Engler's statement that cationic and some of the nonionic detergents "did not have similar effects" (as compared to the dramatic enhancement of gene transfer seen with some of the non-ionic and anionic detergents) does not necessarily imply that the cationic detergents and some of the nonionic detergents have any effects. The statement is also entirely consistent with an interpretation that the cationic and some of the nonionic detergents have no effect on enhancement of gene expression. Taking into account the scoring system used by Engler, the skilled artisan would conclude that the cationic and some of the nonionic detergents had no effect.

Third, the Examiner further contends that Engler teaches, in other portions of the specification, that cationic detergents/surfactants can be used to enhance gene delivery. Yet, the sole mention of cationic detergents (other than in Example 5) is in a laundry list recitation of detergents. See Engler, pg. 5, lines 18-20. There is no indication that a cationic detergent would reasonably be expected to work.

Thus, the Engler reference as a whole does not render *prima facie* obvious an adjuvant comprising a block copolymer and a cationic surfactant. There is simply no motivation to combine Balasubramanian with Engler because Engler does not show any enhancement of gene expression with cationic surfactants. In addition, Engler teaches away from the use of cationic surfactants.

Moreover, even assuming *arguendo* that Engler shows some enhancement of gene expression using recombinant adenoviral vectors, this does not provide any reasonable expectation of success for a polynucleotide vaccine comprising a block copolymer and a cationic

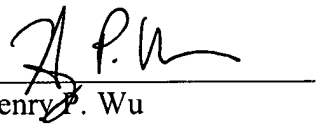
detergent (as claimed in claims 7-13 and 21-26). The invention in Engler is directed to compositions and methods of treating cancer by gene therapy delivered by a gene delivery system. See Engler, pg. 1, lines 10-12. A gene delivery system as contemplated by Engler refers to recombinant viral vector systems (where the viral DNA is encapsulated within a protein coat) and lipid-based systems such as lipid encapsulated DNA and cationic lipid/DNA complexes (where the DNA is encapsulated with lipid). Thus, the DNA described in Engler is protected either by lipid or a protein coat. There is no basis for correlating the results with an adenoviral vector with naked plasmid DNA. Thus, there is no indication that a polynucleotide vaccine formulation with a block copolymer and cationic detergent would reasonably expected to work.

For the above reasons, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. 103.

CONCLUSION

Applicants believe the claims are in condition for allowance. An early indication of the same is requested. The Examiner is invited to contact Applicant's Attorney at the telephone number given below, if such would expedite the allowance of this application.

Respectfully submitted,

Date: January 12, 2009 By: 

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